1148 Myocardial Mechanics and Remodeling in Heart Failure

Tuesday, March 31, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 4:00 p.m.–5:00 p.m.

1148-29 Clinical Correlates and Prognostic Value of Apoptosis Mediator Soluble Forms in Patients With Congestive Heart Failure

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Fas and tumor necrosis factor (TNF) receptors are cell-surface proteins and apoptosis-signaling molecules. To evaluate the role of these apoptosis mediators in the pathophysiology of congestive heart failure (CHF), we determined the serum soluble apoptosis -signaling molecules, such as soluble TNF receptor I (sTNFRI) and soluble Fas (sFas), in 43 patients with CHF (LVEF < 50%; Ischemic heart failure: 31/43; Dilated Cardiomyopathy: 12/43; mild CHF: NYHA I–II, 20/43; severe CHF: NYHA III–IV, 23/43) and 15 healthy age-matched controls using commercially available Elisa tests. CHF patients were also monitored for a follow-up period of more than 6 months. Results showed that serum levels of soluble apoptosis-signaling molecules in CHF patients with ischemic heart failure did not differ significantly from those in CHF patients with dilated cardiomyopathy. Patients with severe CHF exhibited significantly higher serum levels of sTNFRI (4.2 ± 0.9 vs 2.7 ± 0.6 ng/ml, $p < 0.001$) and sFas (5.4 ± 1.3 vs 3.7 ± 0.5 ng/ml, $p < 0.005$) than those of patients with mild CHF and healthy controls (sTNFRI: 1.8 ± 0.1 ng/ml, $p < 0.0001$; sFas: 2.6 ± 0.9 ng/ml, $p < 0.001$). In group of severe CHF patients, serum sTNFRI levels significantly correlated with serum sFas levels ($r = 0.63$, $p < 0.01$), serum sodium ($r = 0.52$, $p < 0.05$) plasma norepinephrine ($r = 0.72$, $p < 0.001$) and LVEF ($r = -0.65$, $p < 0.01$). In the same patients sFas levels also significantly correlated with serum sodium ($r = 0.57$, $p < 0.01$) plasma norepinephrine ($r = 0.68$, $p < 0.01$) and LVEF ($r = -0.55$, $p < 0.05$). Furthermore, in cox proportional hazard models high serum levels of sTNFRI ($p = 0.03$) and sFas ($p = 0.05$) were identified as significant prognostic predictors of 43 CHF patients.

Conclusions: 1) There is a significan relation between the serum levels of apoptosis mediator soluble forms and the severity of CHF despite the cause of the disease. 2) sTNFRI and sFas are markedly elevated and may be associated with the neurohumoral activation and hemodynamic deterioration which were observed in severe CHF patients. 3) sTNFRI and sFas may have a significant prognostic value in CHF.

1148-30 Contractile Reserve Influences Prognosis in Patients With Dilated Cardiomyopathy

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Low-dose dobutamine echocardiographic test (DET) is an accurate method for the detection of myocardial contractile reserve (viability) in coronary artery disease and offers prognostic information. However, this stress modality has not been applied widely in cardiomiopathic states.

To determine the prognostic value of DET in dilated cardiomyopathy, a cohort of 41 pts were followed prospectively after DET. Baseline echocardiographic variables and left ventricular ejection fraction (EF) before and afer 5 infusion of 10 mcg/kg/min dobutamine were collected Clinical and standard echocardiographic data were analyzed at 3-monthly intervals.

During the follow-up of 7–26 months (mean 12±4 months) 5 pts (12%) died, and 11 pts (27%) revealed a decrease of EF. LV diastolic dimension ($p < 0.01$). E/A mitral inflow ratio ($p < 0.05$), and inadequate increase in EF during DET ($p < 0.05$) were independent predictors of death, whereas the baseline EF was not. Only inadequate increase of EF during DET ($p < 0.001$) was a predictor of unfavorable outcome (death or EF decrease). The mean increase of EF after DET was 19 ± 5% and 28 ± 17% of the baseline value in group of pts with unfavorable and favorable outcome, respectively. Using multivariate regression analysis wall thickness (coefficient -0.012, $p < 0.003$), E/A ratio (-0.006, $p < 0.05$), right ventricular dimension (-0.017, $p < 0.05$), and changes of EF after DET (0.02, $p < 0.05$) were found to have a significant association with mortality, that was independent of age, clinical signs and symptoms or baseline ejection fraction. Only the left atrium and right ventricle dimension, and lack of increase of EF after DET had a prognostic value for unfavorable outcome. Additionally, there was a linear regression between increase of EF after DET and changes of EF during follow-up ($y = 0.53x - 0.03$, $r = 0.45$, $p < 0.05$).

Conclusion: Low-dose dobutamine echocardiography provides prognostic information in patients with dilated cardiomyopathy. The single most important independent predictor for unfavorable outcome is an abnormal left ventricular contractile response on dobutamine. Moreover, the extent of the contractile response is major determinant for ejection fraction in the future.

1148-31 Coronary Microcirculation Abnormality Affects Left Ventricular Systolic Function in Idiopathic Dilated Cardiomyopathy (DCM)

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Coronary microcirculation is reported to be impaired in patients with DCM. However, the influence of this abnormality on left ventricular (LV) systolic function has not been fully studied. To assess the relation between coronary microcirculation abnormality and LV contractility, we consecutively performed ^{99m}Tc-sestamibi SPECT and echocardiography during dipyridamole infusion (DIP) in 18 DCM patients with mild heart failure (HF) (Group I, EF >30%, n = 10) and with severe HF (Group II, EF <30%, n = 8). Severity score (SS), a quantitative perfusion marker, %fractional shortening (%FS) and wall motion abnormality score (WMAS) were measured at baseline condition (Baseline) and during DIP.

Results: At Baseline, perfusion defects were observed in all patients. During DIP, SS worsened due to inhomogeneous vasodilatory response in myocardium but %FS and WMAS improved due to β-adrenergic stimuli and/or afterload reduction in both groups. In Group II, severer worsening of SS did cause smaller increase in %FS ($r = -0.75$, $p < 0.02$), although there was not significant correlation between these parameters in Group I. These results suggest that in advanced DCM, additional perfusion defects provoked by DIP may suppress the improvement of LV systolic function.

	HR	SS	%FS	WMAS
Group I Baseline	65	86	19%	29
DIP	78*	145*	23%*	20*
Group II Baseline	69 144†	13%†	34	
DIP	86*	181*	17%*	29*

(* $p < 0.05$ vs Baseline, † $p < 0.05$ vs Group I)

Conclusion: We concluded that coronary microcirculation abnormality affects LV performance in patients with severe heart failure caused by DCM.

1148-32 Shortening-Frequency Relationship in Post-infarct Remodeled Cardiac Myocytes

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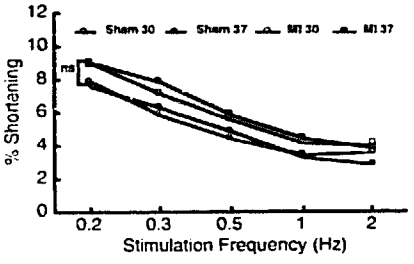
Background: We have shown that myocytes isolated from the regionally dysfunctional hypocontractile segment of non-infarcted LV from post-MI remodeled rat hearts exhibit normal contractile function and $[Ca^{++}]_i$ kinetics. To identify whether increasing frequency of stimulation would unmask any latent myocyte dysfunction, we examined myocyte shortening (video edge detection) and $[Ca^{++}]_i$ (Fura2-AM) in 67 myocytes from 6 MI and 71 myocytes from 11 sham-operated rats. Hearts from MI rats had depressed systolic function (Langendorff LVDP 70 vs 112 mmHg, $p = 0.035$) and their myocytes were longer (126 vs 107 um, $p < 0.01$). Myocytes from these hearts were stimulated from 0.2 to 2 Hz at 30° & 37°C.

Results: A similar frequency-dependent decrease in % shortening, velocity of shortening, amplitude of $[Ca^{++}]_i$ transient and velocity of rise in $[Ca^{++}]_i$ was seen in MI and sham myocytes ($p < 0.001$, ANOVA). The velocity of shortening was higher at 37°C in both I groups ($p < 0.001$, ANOVA).



Conclusion: These data suggest that factors other than myocyte contractile dysfunction contribute to global LV dysfunction in the post-MI remodeled heart.

TUESDAY POSTER